



**NTP**  
National Toxicology Program

# Report on the NTP Technical Reports Peer Review Panel Meeting, April 5, 2011

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BSC Liaison to Peer Review Panel Meeting

NTP Board of Scientific Counselors Meeting

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National Institute of Environmental Health Sciences / National Institutes of Health  
National Institute for Occupational Safety and Health / Centers for Disease Control  
National Center for Toxicological Research / Food and Drug Administration





## Draft Technical Reports Peer Reviewed on April 5

- Senna
- A NondecORIZED Whole Leaf Extract of *Aloe barbadensis* Miller (*Aloe vera*)
- Acrylamide
- Combinations of AIDS therapeutics
  - 3'-azido-3'-deoxythymidine (AZT), lamivudine (3TC), and either nevirapine (NVP) or nelfinavir (NFV)

## Technical Reports Peer Review Panel Roster

John Cullen, VMD, PhD, DACVP, North Carolina State University (Chair)

Lucy M. Anderson, PhD, DABT, Private Consultant

Norman Barlow, DVM, PhD, MBA, MLD, DACVP, DABT, Sanofi-Aventis

Diane Birt, PhD, Iowa State University

Wendy J. Heiger-Bernays, PhD, Boston University School of Public Health

James E. Klaunig, PhD, ATS, Indiana University

Mark S. Miller, MPhil, PhD, Wake Forest University School of Medicine

Arlin Rogers, DVM, PhD, University of North Carolina at Chapel Hill

Mitzi Nagarkatti, PhD, University of South Carolina School of Medicine  
(BSC Liaison)



## Charge

- Peer review the scientific and technical elements of the study and its presentation
- Determine whether the study's experimental design and conduct support the NTP's conclusions regarding the carcinogenic activity of the substance tested



## Levels of Evidence of Carcinogenic Activity

- **Clear evidence of carcinogenic activity**
  - Dose-related (i) increase of malignant neoplasms, (ii) increase of a combination of malignant and benign neoplasms, or (iii) marked increase of benign neoplasms if there is an indication from this or other studies of the ability of such tumors to progress to malignancy
- **Some evidence of carcinogenic activity**
  - Chemical-related increased incidence of neoplasms in which the strength of the response is less than that required for clear evidence
- **Equivocal evidence of carcinogenic activity**
  - Marginal increase of neoplasms that may be chemical related
- **No evidence**
- **Inadequate study**

## Senna

Widely used as a laxative

Based on a 40-week feed study, the panel recommended the conclusions with a 4-2-0 vote, and the NTP accepted the panel's recommendation

| Sex/Species  | Evidence | Neoplastic lesions |
|--|----------|--------------------|
| Male C3B6.129F1- <i>Trp53</i> <sup>tm1Brd</sup> N12 haploinsufficient mice   | NE       | —                  |
| Female C3B6.129F1- <i>Trp53</i> <sup>tm1Brd</sup> N12 haploinsufficient mice | NE       | —                  |

NE = no evidence

## **A Nondecolorized Whole Leaf Extract of *Aloe barbadensis* Miller (*Aloe vera*)**

Plant extract used in alternative medicine and dietary supplements

Based on a 2-year drinking water study, the panel recommended the conclusions as written with a 6-0-0 vote, and the NTP accepted the panel's recommendation

| <b>Sex/Species</b> | <b>Evidence</b> | <b>Neoplastic lesions</b>                         |
|--------------------|-----------------|---|
| <b>Male Rats</b>   | <b>CE</b>       | <b>Adenomas and carcinomas of large intestine</b> |
| <b>Female Rats</b> | <b>CE</b>       |   |
| <b>Male Mice</b>   | <b>NE</b>       | <b>—</b>  |
| <b>Female Mice</b> | <b>NE</b>       | <b>—</b>  |

CE = clear evidence; NE = no evidence

## Acrylamide

A contaminant in baked and fried starchy foods; used in laboratory procedures involving polyacrylamide gels; component of cigarette smoke; exposures in various occupations (monomer production and polymerization reactions)

Based on a 2-year drinking water study, the panel recommended the conclusions with a 6-0-0 vote, and the NTP accepted the panel's recommendation

| Sex/Species | Evidence | Neoplastic lesions  |
|-------------|----------|---|
| Male Rats   | CE       | Malignant mesothelioma of epididymis and testis; malignant schwannoma of the heart; follicular cell adenoma or carcinoma of thyroid gland   |
| Female Rats | CE       | Fibroadenoma of mammary gland; squamous cell neoplasms (primarily papilloma) of oral cavity; mesenchymal neoplasms (fibroma, fibrosarcoma, or sarcoma) of skin; follicular cell neoplasms (adenoma or carcinoma) of thyroid gland |
| Male Mice   | CE       | Neoplasms (primarily adenoma) of harderian gland; alveolar/bronchiolar neoplasms (primarily adenoma) of lung; squamous cell neoplasms (primarily papilloma) of forestomach  |
| Female Mice | CE       | Adenoma of harderian gland; alveolar/bronchiolar adenoma of lung; adenocanthoma and adenocarcinoma of mammary gland; benign granulosa cell neoplasms of ovary; malignant mesenchymal neoplasms of skin                            |

CE = clear evidence



## AIDS Therapeutics

Combination therapies for AIDS

Based on 2-year transplacental gavage studies in B6C3F1 mice, the panel recommended the conclusions (2 yes, 2 no, 1 abstention; the Chair broke the tie with a yes vote), and the NTP accepted the panel's recommendation

| <b>AZT<br/>Therapeutics</b> | <b>Male Mice</b>  | <b>Female Mice</b>  |
|-----------------------------|---|---|
| <b>AZT</b>                  | <b>NE</b>   | <b>EE</b><br><b>Neoplasms (primarily adenoma) in thyroid;<br/>fibrosarcoma or sarcoma in skin</b> |
| <b>AZT + 3TC</b>            | <b>NE</b>   | <b>EE</b><br><b>Alveolar/bronchiolar adenoma of lung</b>  |
| <b>AZT + 3TC + NVP</b>      | <b>SE</b><br><b>Fibroma, fibrous<br/>histiocytoma or<br/>fibrosarcoma in skin</b> | <b>EE</b><br><b>Fibrosarcoma in skin</b>  |
| <b>AZT + 3TC + NFV</b>      | <b>NE</b>   | <b>NE</b>   |

NE = no evidence, EE = equivocal evidence; SE = some evidence